

## Claims

1. A method for increasing or maintaining the number of functional cells of a predetermined type in an organ or tissue of a mammal, wherein said organ or tissue is injured, damaged, or deficient in said functional cells, said method comprising administering to said mammal a composition enriched in pluripotent cells that express the *Hox11* gene.
2. The method of claim 1, further comprising stimulating said organ or tissue before administering said composition.
3. The method of claim 2, wherein said organ or tissue is stimulated by administering TNF-alpha.
4. The method of claim 2, wherein said organ or tissue is stimulated by administering a TNF-alpha agonist or a TNF-alpha inducing substance.
5. The method of claim 4, wherein said TNF-alpha agonist or TNF-alpha inducing substance is Complete Freund's Adjuvant (CFA), ISS-ODN, microbial cell wall components with LPS-like activity, cholera particles, *E. coli* heat labile enterotoxin, *E. coli* heat labile enterotoxin complexed with lecithin vesicles, ISCOMS-immune stimulating complexes, polyethylene glycol, poly(N-2-(hydroxypropyl)methacrylamide), synthetic oligonucleotides containing CpG or CpA motifs, monophosphoryl lipid A, Bacillus Calmette-Guerin,  $\gamma$ -interferon, Tissue Plasminogen Activator, LPS, Interleukin-1, Interleukin-2, UV light, a

lymphotoxin, cachectin, a TNFR-2 agonist, an intracellular mediator of the TNF-alpha signaling pathway, a NFκB inducing substance, IRF-1, STAT1, a lymphokine, or the combination of TNF-alpha and an anti-TNFR-1 antibody.

5        6.        The method of claim 5, wherein said TNF-alpha agonist or TNF-alpha inducing substance is Complete Freund's Adjuvant, Bacillus Calmette-Guerin, or γ-interferon.

10       7.        The method of claim 2, wherein said organ or tissue is stimulated 6-12 hours before administering said composition.

8.        The method of claim 1, wherein said composition is enriched in cells which do not express CD45 protein.

15       9.        The method of claim 8, wherein said pluripotent cells are enriched from the peripheral blood or tissue of a mammal by a method comprising:

- a)        providing from the mammal peripheral blood or tissue that contains pluripotent cells;
- b)        separating pluripotent cells from said peripheral blood or tissue;
- 20       c)        separating said pluripotent cells into a first cell population which expresses CD45 antigen on the surface of said cells and a second cell population which predominantly does not express CD45 antigen on the surface of said cells; and
- d)        selecting said second cell population.

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10. The method of claim 1, wherein said pluripotent cells are derived from the spleen.

11. The method of claim 1, wherein said pluripotent cells are semi-  
5 allogeneic.

12. The method of claim 1, wherein said pluripotent cells are isogeneic.

13. A method for increasing or maintaining the number of functional cells  
10 of a predetermined type in an organ or tissue of a mammal, wherein said organ or tissue is injured, damaged, or deficient in said functional cells, said method comprising administering to said mammal a composition comprising pluripotent cells resulting from transfecting a pluripotent or totipotent cell with a *Hox11* gene.

14. The method of claim 13, wherein said *Hox11* gene is expressed.

15. The method of claim 13, wherein said pluripotent cells are the result of transfecting a pluripotent cell.

16. The method of claim 15, wherein said pluripotent cell is semi-  
20 allogeneic.

17. The method of claim 15, wherein said pluripotent cell is isogeneic.

18. The method of claim 13, further comprising stimulating said organ or  
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tissue before administering said composition.

19. The method of claim 14, wherein said organ or tissue is stimulated by administering TNF-alpha.

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20. The method of claim 14, wherein said organ or tissue stimulated by administering a TNF-alpha agonist or a TNF-alpha inducing substance.

21. The method of claim 20, wherein said TNF-alpha agonist or TNF-alpha  
10 inducing substance is Complete Freund's Adjuvant (CFA), ISS-ODN, microbial cell wall components with LPS-like activity, cholera particles, *E. coli* heat labile enterotoxin, *E. coli* heat labile enterotoxin complexed with lecithin vesicles, ISCOMS-immune stimulating complexes, polyethylene glycol, poly(N-2-(hydroxypropyl)methacrylamide), synthetic oligonucleotides containing CpG or  
15 CpA motifs, monophosphoryl lipid A, MPL, Bacillus Clamette-Guerin,  $\gamma$ -interferon, Tissue Plasminogen Activator, LPS, Interleukin-1, Interleukin-2, UV light, a lymphotoxin, cachectin, a TNFR-2 agonist, an intracellular mediator of the TNF-alpha signaling pathway, a NF $\kappa$ B inducing substance, IRF-1, STAT1, a lymphokine, or the combination of TNF-alpha and an anti-TNFR-1 antibody.

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22. The method of claim 21, wherein said TNF-alpha agonist or TNF-alpha inducing substance is Complete Freund's Adjuvant, Bacillus Clamette-Guerin, or  $\gamma$ -interferon.

25 23. The method of claim 14, wherein said organ or tissue is stimulated 6-12

hours before administering said composition.

24. A pluripotent cell transfected with a *Hox11* gene, wherein said cell is capable of differentiating into a cell selected from the group consisting of : a  
5 pancreatic cell, a spleen cell, a liver cell, a kidney cell, and a bone cell.

25. The cell of claim 24, wherein said cell is capable of differentiating into a pancreatic cell.

10 26. The cell of claim 24, wherein said cell is transfected with a human *Hox11* gene.

27. The cell of claim 24, wherein said pluripotent cell is derived from the spleen.  
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28. The cell of claim 24, wherein said pluripotent cell is derived from cord blood.

29. The cell of claim 24, wherein said pluripotent cell does not express  
20 CD45.

30. The method of claims 1 or 13, wherein said composition comprises cells that present MHC class I and peptide, wherein said MHC class I has at least one allele that matches an MHC class I allele expressed by said mammal.  
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31. A method for increasing or maintaining the number of functional cells of a predetermined type in an organ or tissue of a mammal, wherein said organ or tissue is injured, damaged, or deficient in said functional cells, said method comprising administering to said mammal an agent that induces and/or stimulates  
5 *Hox11*-expressing pluripotent cells.

32. The method of claim 31, wherein said *Hox11*-expressing cells are not bone marrow cells.

10 33. The method of claim 31, wherein said agent is a gene therapy vector comprising a *Hox 11* gene operably linked to a promoter, wherein said vector expresses *Hox 11* in said pluripotent cells.

34. The method of claim 31, said method further comprising:  
15 a) quantitating the number of said *Hox11*-expressing cells before administering said agent; and  
b) quantitating the number of said *Hox11*-expressing cells after administering said agent.

20 35. The method of claim 34, said method further comprising administering an additional amount of said agent if said number of *Hox11*-expressing cells of step a) is less than said number of step b).

36. The method of claim 34, said method further comprising administering a  
25 second agent that induces and/or stimulates pluripotent cells in which the *Hox11*

gene is expressed if said number of *Hox11*-expressing cells of step a) is less than said number of step b).

37. The method of claim 34, said method comprising:

- 5 a) detecting in said mammal a first marker expressed by said *Hox11*-expressing cells and a second marker expressed by a control cell population selected from a non-pluripotent cell population or a second pluripotent cell population that is different from said *Hox11*-expressing cells;
- 10 b) quantitating the number of said *Hox11*-expressing cells and said control cells using said first marker and said second marker, respectively, before administering said composition;
- c) quantitating the number of said *Hox11*-expressing cells and said control cells using said first marker and said second marker, respectively, after administering said composition; and
- 15 d) comparing the ratio of said *Hox11*-expressing cells to said control cells of step b) with the ratio of said *Hox11*-expressing cells to said control cells of step c).

38. The method of claim 37, said method further comprising administering  
20 an additional amount of said agent if said ratio of *Hox11*-expressing cells to control cells of step b) is less than said ratio of *Hox11*-expressing cells to control cells of step c).

39. The method of claim 37, said method further comprising administering a  
25 second agent that induces and/or stimulates pluripotent cells in which the *Hox11*

gene is expressed if said ratio of *Hox11*-expressing cells to control cells of step b) is less than said ratio of *Hox11*-expressing cells to control cells of step c).

40. The method of claim 37, wherein said first marker is the result of *Hox11*  
5 gene expression.

41. The method of claim 37, wherein said first marker is detected by a  
compound that binds to said first marker with a binding constant ( $K_D$ ) of less than  
or equal to 1 micromolar.

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42. The method of claim 41, wherein said first marker is detected by an  
antibody.

43. The method of claim 31, wherein said agent is, or induces in said  
15 mammal, a cytokine, chemokine, or growth factor.

44. The method of claim 43, wherein said cytokine, chemokine, or growth  
factor is selected from the group consisting of: epidermal growth factor (EGF),  
platelet-derived growth factor (PDGF), fibroblast growth factors (FGFs),  
20 transforming growth factor-beta (TGF- $\beta$ ), transforming growth factor-alpha (TGF- $\alpha$ ),  
vascular endothelial growth factor (VEGF), erythropoietin (Epo), insulin-like  
growth factor-I (IGF-I), insulin-like growth factor-II (IGF-II), interleukins, tumor  
necrosis factor-alpha (TNF-  $\alpha$ ), tumor necrosis factor-beta (TNF-  $\beta$ ), interferon-  
gamma (INF- $\gamma$ ), stromal cell-derived factor-1 (SDF-1), and a colony stimulating  
25 factors (CSF).



45. The method of any of the claims 1, 13, and 31, wherein said organ or tissue is, or is part of, the pancreas, the spleen, the liver, the kidney, or the bone.

5        46. The method of claim 45, wherein said organ or tissue is, or is part of, the pancreas.

47. A method for increasing or maintaining the number of functional cells of a predetermined type in an organ or tissue of a mammal, wherein said organ or  
10 tissue is injured, damaged, or deficient in said functional cells, said method comprising administering to said mammal an agent that selectively inhibits, removes, or kills cell populations that interfere with or prevent the trafficking of, differentiation of, or growth of pluripotent cells.

15        48. The method of claim 47, wherein said agent targets a cell population deficient in the expression of CD180.

49. The method of claim 48, wherein said agent is BCG, LPS, a triacetylated lipopeptide, phenol-soluble modulin, or OspA LP from *B. burgdorferi*, a  
20 triacetylated lipopeptide with TLR1 or TLR6, HSP60 with TL4, HSP60, a mannuronic acid polymer, a flavolipin, a teciuronic acid, neumolysin, fimbriae, surfactant protein A, hyaluronan, heparin sulfate or a heparin sulfate fragment, a fibrinogen peptide, beta-defensin-2, flagellin, or imidazolquinoline,

25        50. The method of claim 47, wherein said pluripotent cells express *Hox 11*.

51. The method of claim 47, wherein said pluripotent cells are isogenic.

52. The method of claim 47, wherein said pluripotent cells are semi-  
5 allogeneic.

53. The method of any of the claims 1, 13, and 31, further comprising  
administering to said mammal an agent that selectively inhibits, removes, or kills  
cell populations that interfere or prevent the trafficking of, differentiation of, or  
10 growth of *Hox-11*-expressing pluripotent cells.

54. The method of claim 53, wherein said blood cells are lymphocytes.

55. The method of claim 53, wherein said agent comprises TNF-alpha.  
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56. The method of claim 53, wherein said agent comprises a TNF-alpha  
agonist or a TNF-alpha inducing substance.

57. The method of claim 56, wherein said TNF-alpha agonist or TNF-alpha  
20 inducing substance is Complete Freund's Adjuvant (CFA), ISS-ODN, microbial  
cell wall components with LPS-like activity, cholera particles, *E. coli* heat labile  
enterotoxin, *E. coli* heat labile enterotoxin complexed with lecithin vesicles,  
ISCOMS-immune stimulating complexes, polyethylene glycol, poly(N-2-  
(hydroxypropyl)methacrylamide), synthetic oligonucleotides containing CpG or  
25 CpA motifs, monophosphoryl lipid A, Bacillus Clamette-Guerin,  $\gamma$ -interferon,

Tissue Plasminogen Activator, LPS, Interleukin-1, Interleukin-2, UV light, a lymphotoxin, cachectin, a TNFR-2 agonist, an intracellular mediator of the TNF-alpha signaling pathway, a NFκB inducing substance, IRF-1, STAT1, a lymphokine, or the combination of TNF-alpha and an anti-TNFR-1 antibody.

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58. The method of claim 57, wherein said TNF-alpha agonist or TNF-alpha inducing substance is Complete Freund's Adjuvant, Bacillus Calmette-Guerin, or γ-interferon.

10 59. The method of any of the claims 1, 13, and 31, wherein said mammal has an autoimmune disease.

60. The method of claim 59, wherein said disease is diabetes.

15 61. The method of claim 59, wherein said disease is immunologically-mediated glomerulonephritis.

62. The method of claim 59, wherein said disease is chronic hepatitis, primary biliary cirrhosis, or primary sclerosing cholangitis.

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